tive express of human fiver and as such act more likely to contribute to the C-conductor of atotato in humans. Inter-

usidation of nicoolee (Tables 1 and 2).

Table 1: Cascing furmains by cDM expressed human extractions. Blomphobleosist tall then in the presence of MADPH functor $\pm 5D$, = 5D, = 5M.

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College formation (pask rain" erg")

netabolic transfirmation of aisotine to codmine in mammals is a two-feep reaction. The first step is the catalysis of successive to monthly-b⁻¹-b-nament is at by the microscount eprocheme PKN system (I). The correction of the infinitum too to extinct is instituted by cytowice abshippe, excloses [2]. Since motities has been implicated in manifesting that use of tobiling productly, an embergement of the role of the contrac to become is requered. Although it is undear which unten P450 bezymes are responsible for the metaholism of science with increased cottains formation [3]. Recent work using a Hupoz on brace CDNA emicraion, system has demonstrated that calls which exposs CVP266 subfit the highest rate of Constants of securing [4]. We have studied a cDNA-directed arguments reptore, in

on, P., Janes, A.J. and Colognel, J. 1831. J. 1604. Chem., R. Richel, H., Fish, H. and Kail, G.P. 1982. Abolem. Bisplay. Rec. Compat., 188, 192-199 para Cachan, Personpraise Resert Uni-cheptal Sanon, Te Unionin, Neutotic upor

Server, J.C., Woods, S.R., Haldbook, R.E. or A. 1932. Br. J. Che. Server, J.K., Stockers, C.J., Garcoy, M.J. of S. Welfers, J., Stockers, C.J., Garcoy, M.J. of S. W. Skelen, J., Server, C.J., Garcoy, M.J. of S. W. this wait was poppered by the Souteborn Telenon Rengeria Colonia, UTA.

segme is highly active in the ecoversion of exentne to entitioning expressed in luman from sed on each will be wively misspeciant in the metabolism of skooline in most

mortant to note that CYP2B6 is not

inec. However, Harr

The skillty of quinidare (a specific inhibitor of CYP2D9) tability the correction of nicotine to externe mediated by CYPZDs, and not CYPZBs, confirms the role of this outputs in the Conduction of nicuosite. Bouwert, current ydeoperavide was not specific for the CVP2D6 mediated

Formation by cDNA experies herem systemates Lost these in the presence of contract Aptingensuisk (monet \$ 50; a = 8). Contains formation + Quivides % habbides (prod sin* mg*)

Ser. Const

pocific cusper, systems involved in the necessities of skodne to colaine, phenobarbitans pro-meatment is se-

The state of the s

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which howen Belyaphoblassid cell Rises, engineered to express Hably individual human synochromes PASI «DNA», vas med to determine which PAM incepanes are responsible the metabolism of plactons in rates we have used cither as NADPH generating system or camena hydroperatios. At low concentrations, custom hydroperation copielts the shilts of CYP2D6 to feation as a percargenace and has or the steesbolism of electric to exchang. In order to study

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zively. Analyses were performed using the spelloss

niction tecturque and under these conditions nicotion

.. I and 7.3 with respectively.

ere comfed out in parallel.

CYP286 had the highest niceties Coniderion activity in

icetine (1 mM). Control iscalations without inhibitor were

vial (0.8 mL). The sample was exposated to dynaso, the resistance redused in methods (10 pL) and as Expert (19 pL). and descended and the expanic layer placed in a tapened gias The gas chromatograph was a Hewicti-Packard Model 1901 instrument opiniosed with a aitrogen-plouphoness stend at 26TC and the detector at 28TC. The colonia

letted caso the gas chromatograph.

type: 5 min) the aqueous layer thus remove

Vactorials and antibods: Incolutions for the determination of alcotine C-cusistion activity were in a final volume of 500 pd. A &! M phombate boller pli 7.4 a 37°C. Maroporal post in (100 pd.) and MgCs. (10 mld). Revenions were started by the addition of 1 ml nicotine (50 pd. of 10 ml nicotine 130 pd. of 10 ml nicotine 130 pd. 1 after 20 min by the addition of 5 M NaOH (59 pil.) When the NADPH system was replaced by camera syntoperoxide, incolations were carried out in a link volume of 190 p.L. (O. I. M. phosphate budier p.H. 7.4) at 25°C, Curd OH 190% in camendoli, was diluted dist to 40 m.M. in 59% nethroot is 8,0 (nh) and then to 1,25 mM to 0,1 M hospitate buffer pet 7.4. An aliquot (10 pd.) of this solution ras added to the microscensi suspension before the addition of nicotiste (1 mM), and the reaction was stapped by the addition of 5 m NaOH (50 aL). As a communicate of pontraentat hydrolysis, incubations containing no protein the presence of quinidine (10 pM), a specific inhibition of CYPZD6 [6]. Microsomal process (50 pg) was included with

occe described as being issayme-specific for CNVID6 [5].

he samples were mechanically statem (5 mis). After con

column (10 m x 0.32 man 10). The injection port wa and at 220°C for 5 min, increased from 220-270°C at OV. pain" and then maintained at 200°C for 5 min. The

clocks. Analyzes were performed on a fused

repessions was increased from 100-23°C at 30°C min under pas (betient), indiregen, as and make-up gas (witnigen were used at four rates of 2.5, 10, 135 and 18 pal, max and Wethyl association had retention times of 3.9 bends: Tables I and 2 show that those cells which expresses

4.W. McCachen, S. Chakerma and J.R. M. CYPADS has been extensively studied. 5-10% of a Caucaster egylgiton exhibit a defert in the gane which codes for this sayes, which mades them poor metabolisers of many used sentitions. Although less is known of the actions are that contribute to variable in the expression of CYFZA6 in human fiver specimens, an inactive varient of this coaynes has been identified. Unible CYPZB6, both CYPZA6 and CYPZD6 are coupling ndividual variability in the expression of these coaymen may term important implications for an individually ability to Webert, D.S., Shipenga, M.K. and Catagodi, J. 1991, Ong Mass. Dayer, 11, 615-428 Smaller, A.M. Gelbeit, H.V., Aspers, T. et al 1972. Backers spine, R. and Myor, U.A. 1988. Modess. Photons.

of either oxidam, although the activity sees was CYPECU, 203, 201 or 3A4 showed a lack of woodine C-outdesion activity in the presence of other NADPH or Describes has the ability to inhibit the CYP2D6 mediated anersion of shorting to exclusive completely. However, has no individual effect on the CYP296-mediansk C-Discussions it is now well entablished that inter-bullwidges! majority in the expression of eyochemics PASI has the plantesculogist and textobaped emedjectes. this shedy three P450 incomes, each with known variability a expression in because fiver samples [7], have been shown o mediate the conversion of protine to connine. With men to CVPIBE, the results obtained are in agreement of the of Parmang at al. [4] and indicate that this

meidenship less (ben that with CVP2B6. Octis expressing

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N.W. McCretten, S. Cholerton and J.R. Like

Cofinine formation by cDNA-expressed human cytochromes P450

Mod. Sci. Rev., 1972; 78, 577-573.